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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,481	12/18/2001	Miquel Sales Amill	INL-048	3281

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EXAMINER	
DAVIS, DEBORAH A	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 11/05/2003

/ 6

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/022,481	SALES AMILL ET AL.	
	Examiner	Art Unit	
	Deborah A Davis	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *23-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-17 and 32 in Paper No. 8 is acknowledged. The traversal is on the ground(s) that Group I and II be rejoined because there is not serious burden to justify restriction. This is found persuasive because art applied to claim 1 would also apply to claim 18 and the dependent claims also overlap with Group I. Therefore, Groups I and II will be rejoined and examined. Currently, claims 1-22 and 32 are under consideration.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 14-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claims 14-15 and 17 recite the limitation "the molar ratio" in line 1. There is insufficient antecedent basis for this limitation in the claim.

5. Claim 16 recites the limitation "the amount" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-3, 6-7, 10-13, 18, and 21-22 is rejected under 35 U.S.C. 102(b) as being anticipated by Kenji et al (EP 0 476 545).

Kenji et al anticipates the instant claims by disclosing a method for an immunoassay comprising a first particle (fine particle A) bound to the second member (Anti-IgE) and reacting the them with a sample (serum) to form a first complex (column 7, lines 15-31) with an unbound first member (IgE antigen) present in the sample (column 7, line 20). A second particle (fine particle B) bound to a third member (IgE monoclonal antibody), that is different from the second member because both anti-IgE antibodies recognize different binding sites (column 6, lines 30-40) and being capable of binding to the first member (column 7, lines 15-30). One of the two antibodies is bound together with a fluorescent substance to a fine particle (A) and the other antibody is bound together with a quencher to a fine particle (B) (column 3, lines 36-50). The second particle (fine particle B) bound to the third member (Anti-IgE antibody) is reacted with the sample (IgE antigen) to form a second complex such that two kinds of anti-IgE monoclonal antibodies recognizing different sites forms a sandwich assay (column 4, lines 45-48). The assay was measured at a wavelength of 495nm (column 7, lines 21-

23). Kenji et al discloses various incubation times that were carried out in different examples in the range of 0.5 – 40 minutes, that would satisfy step (b) of claim 1 (column 9, lines 49-58). Although the Kenji et al reference does not specifically recite a composition, the components of the composition as recited in claim 18 are taught by the instant reference such that it teaches a first particle (fine particle A) bound to the second member (anti-IgE) and a second particle (fine particle B) bound to a third member (IgE monoclonal antibody) with both antibodies being different wherein they recognize different binding sites, therefore it is the examiner's position that the Kenji et al reference satisfies the instant claim and all that depend therefrom.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 5-6, 8-9,19-20 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kenji et al in view of Koike et al (USP#5,187,067).

The teachings of Kenji et al are set forth above and differ from the instant claims in not teaching protein S and C4b-binding protein.

However, Koike et al teaches immunological determination of free human protein S (1st member) and C4BP (2nd member) -protein S complex in a sandwich format utilizing monoclonal antibodies affixed to insoluble latex carriers (abstract). This method of detection permit measurement of free human protein S or C4bp-protein S complex in an assay sample (i.e. plasma) with good accuracy without variations in the quality of reagents. Protein S and C4bp-protein S complex can be measured directly, and accurate measurement within short periods of time. The determination methods of this invention permit diagnosis of the conditions of thrombosis having cancer as a basic disease, nephrosis and accurate determination of fibrinolytic state of toxemia of pregnancy (column 3, lines 1-35). Plasma samples were taken from normal healthy subject as well who did not exhibit disease and patients who did (column 15, lines 1-12). Protein S and C4BP-protein S complexes were compared and measured (column 15, lines 15-55). These assays can be formed in a two-step method (sequentially) comprising contacting the sample with the fixed primary antibody and then a second antibody or by a one-step method the secondary antibody simultaneously with the primary antibody (column 4, lines 32-68).

It would have been obvious to one of ordinary skill in the art to modify the assay of Kenji et al to include the detection of protein S and its C4b-binding protein as taught by Koike et al because it offers great advantages to medicine wherein determination of these proteins can permit diagnosis of conditions related to cancer and toxemia in pregnant patients.

11. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kenji et al in view of Noguchi et al (USP#4,843,021).

The teachings of Kenji et al are set forth above and differ from the instant claim in not teaching measuring turbidity.

However, Noguchi et al teaches an immunological assay method wherein the concentration of a substance to be assayed can be determined in several ways, one being and increase or decrease in light scatter which is caused by a change in the turbidity accompanying the formation of an antigen-antibody complex reaction (column 2, lines 1-54). Several instruments can be used for determination of the turbidity or a change therein caused by antigen/antibody complex reaction, such as turbidimeter, spectrophotometer or photometer (column 5, lines 37-56).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Kenji et al to include the measurement of antibody-antigen reaction in a sample as taught by Noguchi et al to detect changes in a sample and be able to calculate the concentration based on the turbidity changes in a sample.

12. Claims 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kenji et al in view of Mischak et al (USP#6,124,430).

The teachings of Kenji et al are set forth above and differ in the instant claims in not teaching molar ratios.

However, Mischak et al teaches immunoassays to quantify protein levels in plasma, serum and whole blood. The assay can be carried out either in a sandwich or competition format (column 7, lines 20-45). In a sandwich type assay, the antibody is normally employed in amounts substantially in molar excess of the maximum amount of protein expected to be in the sample (column 8, lines 1-10). Preferably, the antibodies chosen to carry out the sandwich type assay are selected such that the first antibody, which is brought into contact with the protein in the sample, does not bind all or part of the epitope recognized by the second antibody, thereby significantly interfering with the ability of the second antibody to bind the protein.

It would have been obvious to one of ordinary skill in the art to modify the teachings of Kenji et al to include molar ratios taught by Mischak et al because it is known in the art that when sandwich assays are utilized, different antibodies in molar access such as monoclonal and polyclonal are selected so that both antibodies recognizing the same epitopes with a range in close proximity will not overlap (column 7, lines 20-52).

Conclusion

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A: Luigi Preda (USP#5,780,255) teaches a method for determining thrombotic risk in an individual.

B: James H. Morrissey (USP#5,741,658) teaches a kit for an assay for measuring activated factor VII associated with the risk of thromboembolic disease.

C: Deutz-Terlouw et al (Two ELISA's for measurement of protein S, and their use in the laboratory diagnosis of protein S deficiency, Clinica Chimica Acta, Vol, 186, 1989, pages 321-334)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah A Davis whose telephone number is (703) 308-4427. The examiner can normally be reached on 8-5 Monday thru Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1123.

Deborah A. Davis
CM1, 7D16
October 27, 2003

LONG V. LE
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10/21/03